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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/893,321	06/27/2001	D. Wade Walke	LEX-0195-USA	2099

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LEXICON GENETICS INCORPORATED
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EXAMINER	
LANDSMAN, ROBERT S	

ART UNIT	PAPER NUMBER
1647	16

DATE MAILED: 08/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/893,321	WALKE ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☒ Claim(s) *1 and 3-6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Formal Matters

A. Amendment C, filed 7/15/03, has been entered into the record.

B. Claims 1-4 are pending in the application. In Amendment C, Applicants added new claims 5 and 6. Therefore, claims 1-6 are pending and are the subject of this Office Action.

C. The Examiner notes on the record that Applicants did not use the Examiner's suggestion of replacing the word "drawn" with "selected" in claim 1. However, no objection or rejection is being made since the claim is clear and grammatically correct as written.

D. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Information Disclosure Statement

A. Reference CP on the IDS of Paper No. 6, dated August 16, 2002, has been lined through since an "International Search Report" is not proper subject matter for an IDS. This improper citation was overlooked in the previous Office Action, dated 3/10/03.

3. Title

A. The title remains objected to. Applicants did amend the title to remove the word "novel." However, Applicants chose not to limit the title to polynucleotides since they argue that the present invention discloses both polypeptides and polynucleotides. However, the claims of the present invention are drawn to polynucleotides, not to polypeptides themselves. Therefore, the title should be amended, for example, as suggested by the Examiner on page 2 of the Office Action dated 3/10/03.

4. Claim Objections

A. The objection to claim 2 has been withdrawn since Applicants have replaced the term "shown in" with "of."

B. Claims 3 and 4 remain objected to. Applicants chose not to take the Examiner's suggestion and replace the phrase "first disclosed in" with "of," nor did they provide any arguments as to why they maintained this phrase. The Examiner suggests either amending the claim as suggested on page 2 of the Office Action dated 3/10/03, or removing the word "first."

C. Claim 1 is objected to since the syntax could be improved by removing the word "at" after "comprising." Claims 5 and 6 are objected to since they depend from claim 1.

D. Claims 5 and 6 are objected to since claim 5 should recite "the nucleic acid molecule" instead of "a nucleic acid molecule." Claim 6 is also objected to since it depends from claim 5.

5. Claim Rejections - 35 USC § 101

A. Claims 1-4 remain rejected and new claims 5 and 6 are also rejected under 35 USC 101 for the reasons already of record on pages 2-5 of the Office Action dated 3/10/03. Applicants argue that they have clearly asserted in the title and specification that the presently claimed sequence encode novel human GABA receptors. Applicants also argue that the receptors of the present invention share structural similarity to other GABA receptors and that the functions of GABA receptors are well-known in the art, especially due to their medical relevance, as can be seen, for example, in textbooks. These arguments have been considered, but is not deemed persuasive. Respectfully, though Applicants suggest that the sequence(s) of the present invention encode GABA receptors, this is speculative. There is no data to support this assertion. It cannot be concluded that the proteins of the present invention are GABA receptors simply because the specification states that it is believed to be so. While the functions and relevance of known GABA receptors is well-known in the art, Applicants have still not demonstrated that the proteins encoded by the nucleic acid molecules of the present invention are, in fact, GABA receptors. Therefore, the arguments regarding the well-known function of GABA receptors is not persuasive, nor, respectfully, not pertinent in this situation since, again, the receptors of the present invention have not been shown to be GABA receptors.

Applicants have argued that a GenBank reference teaches a protein which is 99% identical to that of the present invention and that, given this and the use of CDART, the artisan would clearly be able to identify the receptors of the present invention as GABA receptors. However, the reference teaches that the protein is a gamma-1 subunit precursor (GABA(A)). Post-filing references can only be used to support an assertion made in the specification at the time of filing. This is not the case here. Applicants do not disclose in the specification that the proteins of the present invention encode a gamma-1 subunit precursor. Applicants have simply asserted that the proteins of the present invention encode GABA recptors. There is no mention in the specification as to which subunit of the GABA receptor the proteins of the present invention encode, nor that the sequence is a precursor. For these reasons, Applicants'

arguments regarding Example 10 of the Revised Interim Utility Guidelines Training Materials are also not persuasive.

Applicants additionally argue that the references cited by the Examiner (Skolnick, Bork, Doerks, Smith, Brenner and Bork), if anything, support Applicants' assertion that homology can be used to predict the function of a novel protein, or encoding nucleic acid. All of Applicants' points regarding these references have been considered. Taken as a whole, these references show that prediction of novel proteins based on known homologous proteins is, at best, speculative.

Applicants argue that "an invention is useful under section 101 if it is capable of providing some identifiable benefit" and that "any utility of the claimed compounds is sufficient to satisfy 35 USC 101." They also argue that those of skill would only need to find any of the described utilities believable. However, as stated under the current utility guidelines (published 1/5/01, 66 FR 1092), the claimed invention needs to be supported by a specific and substantial asserted utility, or a well-established utility. However, no specific, or substantial benefit has been identified. While those of skill may find the general assertion of a utility believable, the general agreement of utilities the artisan would consider believable does not mean that the present invention has the disclosed utilities simply because they have been asserted by Applicants. Applicants have not taught what the specific function is of the protein encoded for by the nucleic acid molecules of the present invention, nor have Applicants identified a substantial role of this protein; for example, how this specific receptor can be used, or with what diseases this specific protein is associated.

Applicants further cite *In re Brana*, their major argument being that "further research does not preclude a finding that the invention has utility" and that "further research and development" is (may be) necessary. However, In re Brana, as stated by Applicants, is concerned with the utility of *pharmaceutical compositions* whereas the present invention is concerned with receptor *proteins*. In using Applicants' own logic, as seen in the subsequent paragraph regarding Applicants' discussion of the relevance of Brenner v. Manson to the present invention, compounds (and pharmaceutical compositions) are not analogous to receptor proteins. Applicants make no mention in their arguments of Brana that the compounds, themselves, to be used in the pharmaceutical compositions do not have utility. Applicants only state that Brana is concerned with the *pharmaceutical compositions* comprising these compounds. Applicants discuss the significance of the FDA and Phase II testing regarding Brana. However, these issues are not relevant in this situation. If Applicants were claiming that the protein of the present invention, or nucleic acids encoding these proteins, could be used in pharmaceutical compositions, that would be analogous. However, the proteins themselves would first need to possess utility in order for the pharmaceutical

composition to possess utility. Since the proteins of the present invention do not possess utility, any comparison to Brana is, respectfully, irrelevant. As stated on page 3 of the Office Action dated 3/10/03, a patent is not a hunting license. This same statement can be made with regard to Applicants' argument using *In re Angstadt and Griffin*. Applicants state that "the need for some experimentation does not render the claimed invention unpatentable." However, this amount of experimentation required to practice the claimed invention is "undue" since, as discussed throughout this rejection, the only information disclosed in the instant specification is that the protein is believed to be a GABA receptor protein, with no further support of utility.

Furthermore, Applicants argue that Brenner v. Manson is not analogous to the present situation since an activity, such as an anticancer activity, is distinct from a term (i.e. GABA receptor) that defines a molecular function. Applicants argue that GABA receptors have a well-known biological role and that this description is more specific than a general "activity." However, the Examiner maintains that while these examples are not identical, they are, in fact, analogous. If the artisan were to consider "GABA receptor activity" to be analogous to "anticancer activity," as was intended in this analogy, then it can be seen how, simply because one protein or compound was known to have activity, this does not confer activity to other homologous proteins or compounds. Furthermore, the Examiner does not understand how these terms differ, i.e. how one is more general than the other. "GABA receptor activity" is just as general or as specific as "anticancer activity." Both of these terms define a specific function (using specific compounds to mediate specific GABA functions in order to affect specific diseases in cells, such as psychiatric disorders vs. specific drugs which affect specific cancer cells) as well as a general function (the general concept of mediating GABA functions for the purpose of mediating general CNS functions vs. any drug which affects any cancer). These arguments are supported by Siegal et al. as presented by Applicants. Therefore, this situation, as well as the terms "GABA receptor activity" and "anticancer activity" are sufficiently analogous to be pertinent to this rejection. Even if, *arguendo*, these situations were not analogous, homology alone is not a sufficient basis for a determination of utility, as discussed throughout this rejection.

Furthermore, Applicants argue that the nucleic acid molecules of the present invention can be used in gene (DNA) chips and that these chips have substantial industrial utility. They also argue that the protein of the present invention is a G protein-coupled receptor, and, therefore, is a potential drug target and specific marker of the human genome, for chromosome mapping, or for defining exon-splice junctions. Applicants also state that "the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the...arts." However, none of

these assertions are specific to the protein of the present invention, or its encoding nucleic acids. Any nucleic acid can be used in gene chip technology, or as a marker for a specific location on the human genome and the like. Similarly, hundreds of G protein-coupled receptors are known in the art and are used as drug targets. Again, this is not specific to the protein of the present invention. As made in a similar statement above, the fact that this nucleic acid molecule maps to chromosome 4p12 was not disclosed at the time of filing, nor does this knowledge provide any specific or substantial information regarding this chromosome, or the nucleic acid molecule. The argument that the nucleic acid of the present invention is part human genome project is also not persuasive since, while the human genome project as a whole may be useful, a single nucleic acid molecule, such as the one disclosed in this invention, by itself, is not.

Finally, Applicants bring to the Examiner's attention numerous patents on polynucleotide sequences that have not been directly shown to be associated with the function of the protein set forth in the specification and which claim, for example, polynucleotide fragments. These arguments have been considered, but are not persuasive. First, this application was properly examined under, and is consistent with, the current utility guidelines, published 1/5/01, 66 FR 1092. Furthermore, all U.S. Patent are presumed valid, or would not have issued as U.S. Patents. Since the polynucleotides in these patents have utility, fragments of these polynucleotides have utility. It is believed that all pertinent arguments have been addressed.

Therefore, since the nucleic acid molecules of the invention do not possess a specific, substantial and credible asserted utility or a well established utility, the claimed expression vector and cells, or encoding protein, also do not possess utility.

6. Claim Rejections - 35 USC § 112, first paragraph - enablement

A. Claims 1-4 remain rejected and new claims 5 and 6 are also rejected under 35 USC 112, first paragraph, for the reasons already of record on page 5 of the Office Action dated 3/10/03 as well as for the reasons given in the above rejection under 35 USC 101. Applicants argue that the claimed invention is enabled because it has utility as argued previously. Applicants' arguments have been fully considered, but are not found to be persuasive for the reasons discussed above.

B. Claims 3 and 4 remain rejected under 35 USC 112, first paragraph, regarding "80 contiguous bases" of SEQ ID NO:1 or 3 for the reasons already of record on page 6 of the Office Action dated 3/10/03. Applicants have amended the claims to recite "80 contiguous base" instead of "24 contiguous

bases." However, the rejection is still pertinent. Applicants argue that the artisan would easily recognize, and know how to make and use, these nucleic acid fragments, e.g. in gene chips.

These arguments have been considered, but are not deemed persuasive. While the artisan would be able to recognize the sequence of, and make a fragment comprising, at least 80 contiguous bases of SEQ ID NO:1 or 3, the artisan would not know how to make a polynucleotide which either encodes a functional protein, nor would they know how to use these fragments since neither the protein, nor the encoding nucleic acid molecule from which these fragments are derived is enabled. The breadth is, therefore, excessive especially in light of the fact that Applicants provide no guidance or working examples of the nucleic acid molecule of SEQ ID NO:1 or 3, or of the protein which it encodes, nor do they provide any guidance or working examples of nucleic acid molecules which comprise at least 80 contiguous bases of SEQ ID NO:1 or 3. In addition, Applicants do not provide any *function* of these nucleic acid molecules, fragments, or of the proteins which they may encode. Furthermore, it is not predictable to one of ordinary skill in the art what the functions of these nucleic acids, or the proteins which they encode, would be.

Without knowing the function of the protein of the present invention, nor the function of the encoding nucleic acid molecule, the artisan would not know how to use said fragments. Nucleic acid molecules comprising at least 80 contiguous bases of SEQ ID NO:1 or 3 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said nucleic acid molecules, or to SEQ ID NO:1 and 3. Similarly, nucleic acid molecules which comprise at least 80 contiguous bases of SEQ ID NO:1 or 3 may encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:1 or 3. Even if the artisan can literally recognize these fragments by their sequence and can easily physically make such a fragment, the artisan would not know how to use them. To use these fragments in gene chip technology would not be sufficient to enable these fragments since undue experimentation would be required in this procedure due to the lack of guidance and working examples of the functions of these proteins and encoding nucleic acid molecules. It is not known what the significance would be of any data derived from gene chip technology for a fragment of a polynucleotide which has not been enabled. In other words, it is not known what the artisan would do with information received from gene chip studies using a fragment in which no guidance or working examples regarding any function has been provided.

In summary, the breadth of the claims is excessive with regard to Applicants claiming any and all fragments of SEQ ID NO:1 or 3 in which the only limitation is that these molecules comprise at least 80 contiguous bases of SEQ ID NO:1 or 3. Furthermore, there is a lack of any functional information, via

guidance and working examples, regarding these proteins and encoding nucleic acid molecules as well as the lack of any disclosure as to what critical residues or bases are required to maintain protein or polynucleotide function. These factors, along with the lack of predictability to one of ordinary skill in the art as to what the function of these nucleic acid molecules are, or of the proteins which they may encode, leads the Examiner to maintain that undue experimentation would still be necessary to practice the invention as claimed. It is believed that all pertinent arguments have been addressed.

7. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 3 and 4 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on page 7 of the Office Action dated 3/10/03. The Examiner appreciates Applicants clarification that claims 3 and 4, and not claims 1 and 3, were intended to be the subject of the rejection. Applicants point out that case law only requires that applicants must convey their invention with "reasonable clarity to those skilled in the art" and that a nucleotide sequence is sufficient to satisfy the written description requirement. Applicants argue that, in contrast to Eli Lilly, the present situation discloses "the sequence itself" and that the artisan would be able to distinguish the claimed nucleic acids from others based on the specific structural description provided. They argue that nucleic acid molecules which do not comprise at least 80 contiguous bases of SEQ ID NO:1 or 3 lie outside the claimed genus. Applicants also argue that various U.S. Patents also recognize this phrase regarding "contiguous bases."

These arguments have been considered, but are not deemed persuasive. First, this application was properly examined under, and is consistent with, the current utility guidelines, published 1/5/01, 66 FR 1092. Furthermore, all U.S. Patent are presumed valid, or would not have issued as U.S. Patents. Regarding the case law and the conclusion that the artisan would recognize the genus of nucleic acid molecules claimed, Applicants have not adequately described this genus. Though Applicants have disclosed a nucleic acid sequence itself, they have not disclosed a representative number of examples to adequately describe this genus. The only structural description provided is that the molecules must comprise at least 80 contiguous bases of SEQ ID NO:1 or 3. Nucleic acid molecules comprising at least 80 contiguous bases of SEQ ID NO:1 or 3 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said nucleic acid molecules, or to SEQ ID NO:1 and 3. Similarly, nucleic acid molecules which comprise at least 80 contiguous bases of SEQ ID NO:1 or 3 may encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:1 or 3 and many nucleic acid molecules would have additions to the 3' or 5'

regions of these nucleic acid fragments. Therefore, the genus would include thousands of nucleic acid molecules Applicants have not identified what the function of these nucleic acid molecules is in order to characterize and limit this genus to what has been adequately described in the specification. Therefore, the artisan would not be able to identify molecules which lie outside this genus. It is believed that all pertinent arguments have been addressed.

8. Claim Rejections - 35 USC § 112, second paragraph

A. The rejection of claim 2 under 35 USC 112, second paragraph, has been withdrawn in view of Applicants' amendment to the claim to recite hybridization conditions.

B. The rejection of claim 2 under 35 USC 112, second paragraph, is withdrawn in view of Applicants' amendment to the claim which recites that the nucleic acid molecule hybridizes to the complement of SEQ ID NO:1.

9. Claim Rejections - 35 USC § 102

A. The rejection of claims 3 and 4 under 35 USC 102 as being anticipated by Ymer et al. has been withdrawn in view of Applicants' amendment to the claims to recite that the nucleic acid molecule be at least 80 contiguous bases of SEQ ID NO:1. Ymer et al. does not teach this limitation. Though moot, the Examiner noticed that this rejection (page 8 of the Office Action dated 3/10/03) accidentally recites an additional reference to Hillier et al. However, this was an error on the part of the Examiner. The reference should have been to Ymer et al, as is clear in the first line of the rejection and is clear from Applicants' absence of a discussion of this issue.

10. Conclusion

A. No claim is allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
August 15, 2003

ROBERT LANDSMAN
PATENT EXAMINER